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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,408	SUTHANTHIRAN ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *3-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The examiner of the application has changed. This case has now been transferred as of 4/20/2006. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Brandon Fetterolf, Group Art Unit 1642.

Election/Restrictions

The Election filed on February 27, 2006 in response to the Restriction Requirement of 11/22/2005 has been entered. Applicant's election, without traverse, of Group VIII, claims 1-2 and 13-14, as specifically drawn to a method for reducing or preventing formation or metastasis of a neoplasm in a mammal comprising treating the mammal with an effective amount of an angiotensin II inhibitor, wherein the inhibitor is a small molecule has been acknowledged.

Because Applicants elected Group VIII without traverse, the restriction requirement is therefore deemed to be proper and is made FINAL.

Claims 1-14 are currently pending.

Claims 3-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-2 and 13-14 are currently under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 10/31/2003 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

The disclosure is objected to because of the following informalities:

The specification on page 1 should be amended to reflect the current priority status of the present application, for example: This application is a divisional of U.S. Application Serial No. 09/78 1,146 filed on February 9, 2001, now US Patent 6,641,811. The specification of U.S. Application Serial No. 09/781,146 is hereby incorporated by reference in its entirety.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of compounds that inhibit angiotensin II, e.g. antagonize angiotensin, thereby reducing the formation, progression or metastasis of a neoplasm including. Claim 13 further limits the genus of angiotensin II inhibitors/antagonists to a subgenus of small molecules. Therefore, the claims encompass a genus of molecules defined solely by its principal biological property, which is simply a wish to know the identity of any material with that biological property. However, the written description in this case only reasonably conveys two species of angiotensin II inhibitor which reduces the progression or metastasis of a neoplasm, wherein the angiotensin inhibitors are Losartan and Enalapril.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical

properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 5, paragraph 0023) that angiotensin II inhibitors in accordance with the methods of the invention can be any molecule including, but not limited to, biological molecules as well as small molecules. With regards to the biological molecules, the specification teaches that biological molecules include all lips and polymers of monosaccarides, amino acids and nucleotides (page 5, paragraph 0024). For example, the specification teaches that the biological molecules may be antibodies such as hose disclosed in US Patent 4,780,401, angiotensin II receptors and/or fragments thereof, or antisense and sense nucleic acid molecules (page 5 paragraph 0024, 0025 and page 6, paragraph 0026, 0027, 0028). With regards to the small molecules, the specification teaches (page 6, paragraph 0029) that any molecule that is not a biological molecule is considered a small molecule, wherein their molecular weight is less than 450. As such, the specification teaches (page 6, paragraph 0029) that the small organic molecule includes not only amino acids and nucleotides, but also, organic compounds, inorganic compounds or organometallic compounds. Specifically, the specification (Page 7, paragraph 0033 to page 8, paragraph 0037) teaches that small molecules includes, but is not limited to, Losartan, Salalasin, ES-8891 ... and those disclosed in a variety of US Patents, e.g. 4,168,267 and 5,608,075 to name a few. Thus, while the specification teaches that the angiotensin II inhibitor can be <u>any</u> molecule including any biological molecule or small molecule, the specification (page 16, paragraph 0069 to page 18, paragraph 0073) only appears to reasonably convey two species of angiotensin II inhibitor which reduces the progression or metastasis of a neoplasm, wherein the angiotensin inhibitors are Losartan and Enalapril. A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of angiotensin II inhibitors, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only two species of angiotensin II inhibitors which reduces the progression or metastasis of a neoplasm, wherein the angiotensin inhibitors are Losartan and Enalapril., but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-2 and 13-14 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for reducing formation, progression or metastasis of a neoplasm in a mammal, comprising administering the mammal with an effective amount of a angiotensin II inhibitor, does not reasonably provide enablement for a method of preventing formation, progression or metastasis of a neoplasm in a mammal, comprising administering an effective amount of a angiotensin II inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the nature of the invention, (2) the relative skill of those in the art, (3) the breadth of the claims, (4) the amount or direction or guidance presented, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the state of the prior art, and (8) the predictability or unpredictability of the art.

Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where

no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406) Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

The nature of the invention

The claims are drawn to a method for reducing or preventing formation, progression, or metastasis of a neoplasm in a mammal, comprising administering an effective amount of an angiotensin II inhibitor, wherein the treatment is not part of a chemotherapy or radiation therapy treatment regimen. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Level of skill in the art

The level of skill in the art is deemed to be high, generally that of a PhD or MD.

The breadth of the claims

Applicants broadly claim a method for reducing or preventing formation, progression, or metastasis of a neoplasm in a mammal, comprising administering an effective amount of an angiotensin II inhibitor, wherein the treatment is not part of a chemotherapy or radiation therapy

treatment regimen. The claims are further drawn to a method for reducing or preventing formation, progression, or metastasis of a neoplasm in a mammal, comprising administering an effective amount of an angiotensin II inhibitor, wherein the treatment is not part of a chemotherapy or radiation therapy treatment regimen, wherein the angiotensin II inhibitor is a small organic molecule.

Guidance in the specification and Working Examples

The specification teaches that Losartan, an angiotensin II blocker, reduces pulmonary metastasis in SCID-beige mice (page 16, Example 1). The specification further teaches that Enalapril, an ACE inhibitor, reduces the incidence of tumors as compared to controls (page 17, Example 3). Aside from these two embodiments of the disclosure, the specification is devoid of any models or experimental analysis that reasonably suggests that the claimed method would predictably prevent the formation of tumors in a mammal. Therefore, coupled with the unpredictability of preventing cancer, as underscored by the prior art below, the criticality of providing workable examples in an unpredictable art, such as in cancer prevention, is required for the practice of the instant invention.

Quantity of experimentation

The quantity of experimentation in the areas of cancer prevention is extremely large given the fact that no known cure or preventive regimen is currently available for cancer.

The unpredictability of the art and the state of the prior art

The state of the art at the time of filing was such that one of skill could recognize that angiotensin II inhibitors could be used for the treatment of cancer, e.g. neoplasia. For example, Olga et al. (J. Clin. Invest. 1996; 98: 671-679, *IDS*) teaches that Captopril, an inhibitor of angiotensin converting enzyme, inhibits angiogenesis and slows the growth of experimental tumors in rats. Moreover, Olga et al. teach that because Captopril inhibits neovascularization, patients who are on long term captopril therapy may derive unexpected benefits from its antiangiogenic activities (abstract). Moreover, Dudley et al. (US 5,444,069, 1995) teach imidazo-pyridine derivatives as angiotensin II antagonist. Specifically, the patent teaches that in addition to being useful for the treatment of memory loss, there angiotensin II antagonist are also useful for the treatment of brain

cancer and other cancers, wherein the AT2 receptor is prevalent (column 2, lines 10-11). Thus, these references demonstrate that angiotensin II inhibitors are useful at treating various forms of cancer. However, these references, as well as the prior art, are silent on the use of any compound, including an angiotensin inhibitor, for the prevention of cancer. For example, Pfeffer et al. (New England Journal of Medicine 1992; 327: 669-677) teach the effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Specifically, Pfeffer et al. teach that there was no difference in death between groups receiving the placebo and those receiving captopril with regards to deaths due to cancer, including gastrointestinal cancer (page 671, Table 1 and paragraph bridging column 1 and column 2).

In the instant case, those of skill in the art recognize that reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. Further, such studies require the appropriate experimental models for analyzing chemo- or immunoprevention. For example, Granziero *et al.* (Eur. J. Immunol. 1999, 29:1127-1138) teach that many models are not suitable for testing immunotherapeutic approaches intended to cure cancer. They suggest that the optimal model (prostate cancer, in their case) would have spontaneous tumor development in its natural location (1st column, page 1128) wherein disease progression would closely resemble the progression of the particular type of cancer. Hence, depending on the type of model employed one could establish a reasonable link between antecedent drug and subsequent knowledge of the prevention of the disease. Further, reasonable guidance with respect to correlating agents that prevent cancer may depend upon quantitative analysis from defined populations that have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, or family histories. For example, Byers, T. (CA Journal, Vol. 49, No. 6, Nov/Dec. 1999) teaches that randomized controlled trials are commonly regarded as the definitive study for proving causality (1st col., p.358),

and that in controlled trials the random assignment of subjects to the intervention eliminates the problems of dietary recalls and controls the effects of both known and unknown confounding factors. Further, Byers suggests that chemo-preventative trials be designed "long-term" such that testing occurs over many years (2nd col., p. 359). In addition, a preventive administration also must assume that the therapeutic will be safe and tolerable for anyone susceptible to the disease.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Olga et al. (J. Clin. Invest. 1996; 98: 671-679, *IDS*).

Olga et al. teach that Captopril, an inhibitor of angiotensin converting enzyme, inhibits angiogenesis and reduces the growth of experimental tumors in rats. For example, the reference teaches that systemic administration of captopril slowed the overall growth of angiogenesis-dependent fibrosarcomas growing subcutaneously (page 678, 1st column, 1st full paragraph). Thus, Olga et al. concludes that it is possible that for many patients taking capritol for its hypotensive action, the drug may have a hidden dividend, providing via its antiangiogenic activities a modest decrease in the incidence or severity of a variety of angiogeneisis-dependent diseases including neoplasia (page 678, 1st column, last paragraph). Thus, while Olga *et al.* do not specifically characterize Captopril as an antagonist of angiotensin II, the claimed functional limitation would be

an inherent property of the referenced method since the specification discusses (page 7, paragraph 0034) that Captopril is a small molecule angiotensin II antagonist. Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Claims 1-2 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Dudley et al. (US 5,444,069, 1995).

Dudley et al. teach imidazole-pyridine derivative which act as angiotensin II antagonist (Title). The patent further teaches that in addition to being useful for the treatment of memory loss, there angiotensin II antagonist are also useful for the treatment of brain cancer and other cancers, wherein the AT2 receptor is prevalent (column 2, lines 10-11). For example, the patent teaches that the imidazole-pyridine derivatives can be used in a method of reducing the action and/or growth of neuronal tumors (column 4, lines 26-35).

Claims 1-2 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ashton et al. (WO 92/20661, 1992).

Ashton et al. teach diacylpiperazine derivaties which act as angiotensin II antagonist and are selective to the type 2 (AT2) subtype (abstract). The WO document further teaches a method of inhibiting the growth of neuronal tumor cells which contain AT2 receptors in a patient comprising administering an effective amount of the angiotensin II antagonist (page 141, lines 26-30). With regards to the patient, the WO document teaches that the patient includes, but is not limited to, humans (page 43, line 23).

Claims 1-2 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Edgar et al. (US 5,824,696, 1998).

Edgar et al. teach a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist (column 1, lines 66 to column 2, line 1). Specifically, the patent teaches a method of treating disorders such as tumor growth, i.e., neoplastic transformation and growth/metastasis

(column 2, lines 6-12). With regards to the angiotensin II receptor antagonist, the patent teaches that angiotensin antagonists include, but are not limited to, losartan (column 3, lines 14-17).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olga et al. (J. Clin. Invest. 1996; 98: 671-679, *IDS*) in further view of Edgar et al. (US 5,824,696, 1998).

Olga et al. teach, as applied to claims 1-2 and 13 above, that Captopril, an inhibitor of angiotensin converting enzyme which is used clinically to manage hypertension and congestive heart failure, inhibits angiogenesis and slows the growth of experimental tumors in rats. For example, the reference teaches that systemic administration of captopril slowed the overall growth of angiogenesis-dependent fibrosarcomas growing subcutaneously (page 678, 1st column, 1st full paragraph). Thus, Olga et al. concludes that it is possible that for many patients taking capritol for its hypotensive action, the drug may have a hidden dividend, providing via its antiangiogenic activities a modest decrease in the incidence or severity of a variety of angiogeneisis-dependent diseases including neoplasia (page 678, 1st column, last paragraph).

Olga et al. does not explicitly teach administration of the angiotensin II antagonist to a human.

Edgar et al. teach a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist (column 1, lines 66 to column 2, line 1). Specifically, the patent teaches a method of treating disorders such as tumor growth, i.e., neoplastic transformation and growth/metastasis (column 2, lines 6-12). With regards to the angiotensin II receptor antagonist, the patent teaches that angiotensin antagonists include, but are not limited to, losartan (column 3, lines 14-17).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer the angiotensin II antagonists as taught Olga et al. to a human patient in view of Edgar et al.'s teachings that angiotensin II receptor antagonist can be used to treat tumor in a human. One would have been motivated to do so because Edgar et al. teaches the successful treatment of humans using an angiotensin II receptor antagonist. Moreover, as taught by Olga et al., Captopril is already widely used clinically to manage hypertension and congestive heart failure (page 671, abstract). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering an angiotensin II receptor antagonist as taught by Olga et al. to a human in view of Edgar et *al.*, one would achieve a method for treating cancer in a human.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dudley et al. (US 5,444,069, 1995) in further view of Edgar et al. (US 5,824,696, 1998).

Dudley et al. teach, as applied to claims 1-2 and 13 above, imidazole-pyridine derivatives that act as angiotensin II antagonist (Title). The patent further teaches that in addition to being useful for the treatment of memory loss, there angiotensin II antagonist are also useful for the treatment of brain cancer and other cancers, wherein the AT2 receptor is prevalent (column 2, lines 10-11). For example, the patent teaches that the imidazole-pyridine derivatives can be used in a method of blocking the action and/or growth of neuronal tumors (column 4, lines 26-35).

Dudley et al. does not explicitly teach administration of the angiotensin II antagonist to a human.

Edgar et al. teach a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist (column 1, lines 66 to column 2, line 1). Specifically, the patent teaches a method of treating disorders such as tumor growth, i.e., neoplastic transformation and growth/metastasis (column 2, lines 6-12). With regards to the angiotensin II receptor antagonist, the patent teaches that angiotensin antagonists include, but are not limited to, losartan (column 3, lines 14-17).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer the angiotensin II antagonists as taught by Dudley et al. to a human patient in view of Edgar et al.'s teachings that angiotensin II receptor antagonist can be used to treat tumor in a human. One would have been motivated to do so because Edgar et al. teaches

the successful treatment of humans using an angiotensin II receptor antagonist. Moreover, as taught by Olga et al., Captopril is already widely used clinically to manage hypertension and congestive heart failure (page 671, abstract). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering an angiotensin II receptor antagonist as taught by Dudley et al. to a human in view of Edgar et *al.*, one would achieve a method for treating cancer in a human.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2 and 13-14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-8 and 10 of U.S. Patent No. 6,641,811.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus.

The method for reducing formation, progression or metastasis of a neoplasm in conjunction with immnosuppressive therapy in a mammal in need thereof, comprising treating the mammal with an effective amount of an angiotensin II receptor blocker, e.g. species, claimed in the conflicting patent appears to fall with in the same scope of a method for reducing formation, progression or

metastasis of a neoplasm, comprising administering an effective amount of an angiotensin II inhibitor, e.g., genus, claimed in the instant application.

Note: The transitional term "comprising" recited in the currently pending claims, which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Weichert et al. (US 6,001,881, 1999, cited in the specification on page 7, paragraph 0033) teach a method of treating a disease in which cell proliferation constitutes a primary and secondary cause comprising administering a therapeutically effective amount of a benzoylguanidine derivative, wherein the disease which cell proliferation constitutes a primary and secondary cause is cancer (column 14, lines 17-21 and 28-30).

Walsh et al. (British Journal of Pharmacology 1997; 120: 1302-1311) teach that AII, *angiotensin II*, angiogenesis was inhibited by daily doses of the selective non-peptide At1 receptor antagonist losartan (abstract).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF
April 26, 2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER